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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/606,422	06/26/2003	David F. McComsey	ORT-1222 USA DIV	6306

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EXAMINER	
LUKTON, DAVID	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 01/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/606,422	MCCOMSEY ET AL.	
	Examiner	Art Unit	
	David Lukton	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Pursuant to preliminary amendment, claims 1-9 have been cancelled, and claims 10, 11, 14 and 15 amended. Claims 10-17 are pending.

✧

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants have provided data (page 9+) which indicates that some binding to the thrombin receptor occurs with several of the claimed compounds. Presumably this was assessed by displacement of Ser-(pF)Phe-Har-Leu-Har-Lys-Tyr-NH_2 from "CHRF" membranes. Applicants have also shown inhibition of thrombin-induced platelet aggregation. Based on this, the examiner will stipulate that inhibition of platelet aggregation will occur within a mammal, and that thrombin receptor binding will occur *in vivo* as well. However, these experiments are not tantamount to a showing of therapeutic efficacy. Even if platelet aggregation is mitigated to some extent, it does

not follow therefrom that there exists any disease for which benefit will accrue to the patient who is afflicted with excess platelet aggregation. First, the excess platelet aggregation may not be the sole cause of the disease to begin with, and second, there is no assurance that the extent of the inhibition will be sufficient to overcome the adverse effects of the disease. It is recognized also the the thrombin receptor is involved in a diverse array of biochemical processes. However, it is not evident that success at treating a human disease has ever been achieved with a thrombin receptor antagonist, and even if some success has been achieved in this regard, the assumption would be that the claimed compounds are not as effective at antagonizing the thrombin receptor as that of the prior art compounds. In addition there is the matter of bioavailability and pharmacokinetics, which are likely to be different between compounds.

As stated in *Ex parte Forman* (230 USPQ 546, 1986) and *In re Wands* (8 USPQ2d 1400, Fed. Cir., 1988) the factors to consider in evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims. As it happens, one cannot "predict" therapeutic efficacy in the treatment of thrombin-mediated disorders based solely on the observation that a compound can bind to the thrombin receptor, or inhibit platelet

aggregation. "Undue experimentation" would be required to practice the claimed invention.

In addition to the foregoing, there is the matter of "modulation". Claim 10 could be interpreted to mean that the compounds of formula (1) can "modulate" the thrombin receptor. The term "modulate" would imply both an antagonism and an activation of the receptor. While it may be that one or the other can be achieved, it is far from apparent how applicants intent to simultaneously antagonize and activate the receptor.

✧

Claims 10-17 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Claim 10 recites "treating a condition mediated by modulation of the thrombin receptor". This renders the claim indefinite as to whether the condition *per se* is mediated by modulation of the receptor, or whether it is the treatment that is mediated by modulation of the receptor.

- Claim 10 recites "treating a condition mediated by modulation of the thrombin receptor". Is "modulation of the ...receptor" (claim 10) intended to refer to antagonism of the receptor, or activation, or both?

- Claim 11 asserts that wound healing and tissue repair are "conditions" mediated by the thrombin receptor, and that these conditions (wound healing and tissue repair) can be successfully treated by administering a compound of formula 1. While it may turn out, at some point in the future, that wound healing and tissue repair can be promoted, or even accelerated, the fact remains that wound healing and tissue repair are not diseases; if anything, they would be more appropriately characterized as the antithesis of disease. (See also claim 15).

- Claim 12 recites the term "about" in reference to a range, thus rendering the claim indefinite as to the upper and lower limits of the range.

- Claim 13 recites the term "about" in reference to a range, thus rendering the claim indefinite as to the upper and lower limits of the range.

- In claim 14, the phrase "the composition of claim 10" lacks antecedent basis.

- Claim 16 recites the term "about" in reference to a range, thus rendering the claim indefinite as to the upper and lower limits of the range.

- Claim 17 recites the term "about" in reference to a range, thus rendering the claim indefinite as to the upper and lower limits of the range.

*

The "Hungarian Search Report" was stricken from the IDS. Sufficient information should be provided so that others can obtain the document in question after the patent issues. The remaining references that were stricken from the IDS were so treated because they were not received, and the parent application (09/565715) is not available.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber, can be reached at 571-272-0925. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.